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Neuroprotective Effects of *Coptidis rhizome chinensis* Franch.(Huang Lian)

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Abstract

Coptidis chinensis rhizoma Franch. (CR, Huanglian) is traditionally used alone or in combination with other herbs for the treatment of inflammatory diseases and diabetes, but activities of CR alkaloids also include neuroprotective, neuroregenerative and anti-oxidative effects and there is rising evidence that CR is effective for the treatment of neurodegenerative diseases associated with oxidative stress. We investigated the neuroprotective properties of *Coptidis rhizoma* watery extract (CRE), as well as CR's main alkaloids (berberine, coptisine, jatrorrhizine and palmatine) and its potential mechanism of action. The antioxidant effect was determined by oxygen radical absorbance capacity assay (ORAC) and 2,2-Di(4-tert-octylphenyl)-1-picrylhydrazyl free radical scavenging assay (DPPH). Results from ORAC assay showed a high oxygen radical absorbance capacity for CRE, coptisine and jatrorrhizine. DPPH assays showed strong concentration dependent antioxidant activity of CRE and berberine. Human SH-SY5Y neuroblastoma cells pretreated with CRE and coptisine for two or twenty-four hours ahead of t-BOOH exposure showed a significant increase in cell viability, lower rates of apoptosis and elevated mitochondrial membrane potential levels with the largest effect after 24 hours of pretreatment; however, ROS production was not changed significantly. Elisa-Assay and qRT-PCR analyses revealed that the expression of the TXNIP gene was down regulated by CRE and coptisine, as the main single component responsible for the neuroprotective effect of CRE. Furthermore the neuroprotective effect of CR in-vitro and in-vivo was tested in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) and 1-methyl-4-phenylpyridinium (MPP⁺, the active metabolite of MPTP) models of Parkinson's disease (PD). MPP⁺ treated human SH-SY5Y neuroblastoma cells were used as cell model. 24 hours pre-treatment of the cells with the CRE significantly increased cell viability as well as intracellular ATP concentration and attenuated apoptosis compared to MPP⁺ control. Further experiments with the main alkaloids of CR, berberine, coptisine, jatrorrhizine and palmatine revealed that berberine and coptisine were the main active compounds which were responsible for the observed neuroprotective effect. However, the full extract of CR was more effective than the tested single alkaloids. In the MPTP induced animal model of PD, CR improved dose-dependently motor functions and increased tyrosinhydroxylase-positive neurons in the substantia nigra. Improvement of NCS may represent an acupuncture induced regeneration, so acupuncture treatment should be a considered as a relevant treatment option in peripheral neuropathy. Due to its neuroprotective properties CRE and its main active alkaloids coptisine and berberine might be potential therapeutic agents for the prevention or amelioration of neurodegenerative disorders.